OCULAR MANIFESTATIONS OF INTRACRANIAL CHORDOMAS*

BY *Steven M. Bagan,* MD (BY INVITATION)
AND *Robert W. Hollenhorst,* MD

CHORDOMA IS AN UNCOMMON NEOPLASM THAT ARISES FROM NOTOCHORDAL remnants embedded in bone along the spinal column and skull base. Although chordomas may arise anywhere from the sella turcica to the coccyx, they most often arise either in the sacrococcygeal area or from the clivus. The clivus is that portion of the cranial floor formed by the basilar parts of the occipital and sphenoid bones, from the foramen magnum to the dorsum sellae.

Chordomas are gelatinous, grayish tumors composed of cells varying from spindle cells to the characteristic vacuolated physaliphorous cells. These mucin-containing cells are suspended in varying amounts of extracellular mucin (Fig 1).

Because of their proximity to the brainstem and their tendency for slow growth and local invasion along the floors of the middle and posterior fossae, clival chordomas frequently involve cranial nerves. This study was undertaken to determine the incidence of various ocular findings in patients with intracranial chordomas. Chordomas not arising intracranially were excluded from this study.

MATERIALS

The data, drawn from the files of the Mayo Clinic, included material from all patients who came for initial diagnosis or treatment of intracranial chordoma. Excluded were patients who had initially been treated elsewhere and had come to us because of recurrence and patients in whom the diagnosis could not be assured.

Sixty-three patients seen between 1932 and 1978 are included in the study. Of these, 61 had tissue-confirmed diagnosis, whereas in the two others, the diagnosis was established by characteristic clinical and radiographic findings but an operation was not performed. Data on many of these patients were included in an earlier report from this institution.[1]

*From the Department of Ophthalmology, Mayo Clinic and Mayo Foundation.

TR. AM. OPHTH. SOC. vol. LXXCVIII, 1980

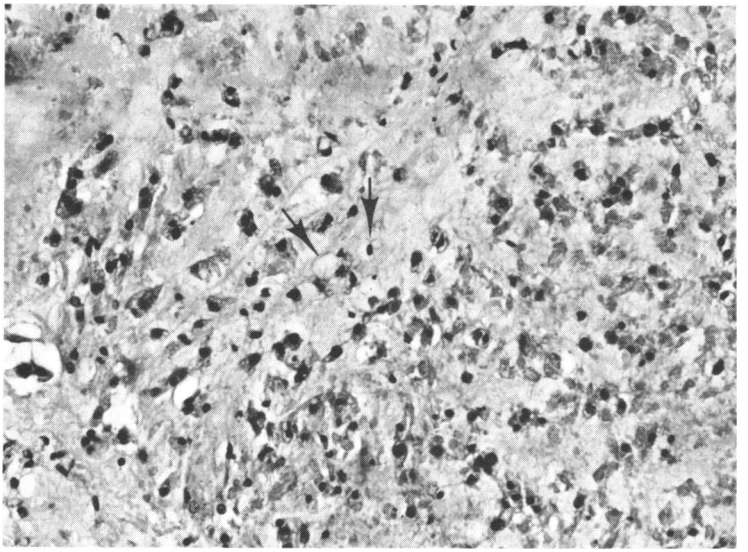

FIGURE 1
Intracranial chordoma. Arrows show physaliphorous cells (hematoxylin and eosin, ×250).

RESULTS

The 63 patients ranged in age from 8 to 91 years; the average age was 44 years. The study group included 37 (59%) male and 26 (41%) female patients.

Most patients had multiple complaints when first seen. The most common symptoms were diplopia (70%) and headache (57%)—14 patients had only these two symptoms. Other symptoms commonly noted were ataxia (17%), decreased visual acuity (16%), weakness of an extremity (11%), and dysphagia (11%); less common symptoms were blepharoptosis, nasal discharge or obstruction, dysarthria, nausea and vomiting, facial numbness, deafness, weakness of facial muscles, tongue weakness, vertigo, vocal cord paralysis, visual field loss, and hypopituitarism (Table I).

The most common symptom of the 10 patients who initially had only one symptom was diplopia (16%). Two patients had only nasal discharge, two had only headache, and three had only decreased visual acuity.

The duration of symptoms ranged from 2 weeks to 10 years. Most patients were seen from 6 months to 3 years after onset of symptoms.

TABLE I: INITIAL SYMPTOMS IN 63 PATIENTS WITH INTRACRANIAL CHORDOMAS

Symptom	Number of patients	Percent
Diplopia	44	70
Headache	36	57
Ataxia	11	17
Decreased vision	10	16
Weakness of extremity	7	11
Dysphagia	7	11
Blepharoptosis	5	8
Nasal discharge or obstruction	5	8
Dysarthria	4	6
Nausea and vomiting	4	6
Facial numbness	4	6
Deafness	3	5
Facial weakness	3	5
Tongue weakness	3	5
Vertigo	2	3
Vocal cord paralysis	2	3
Visual field loss	2	3
Hypopituitarism	2	3

In 39 (62%) patients, the initial symptom was ocular (diplopia, visual loss, field loss, blepharoptosis), and in another three (5%), ocular symptoms were noted simultaneously with other symptoms.

The frequency with which the various initial ocular findings occurred is listed in Table II. Vision was normal in 46 patients (73%); the decreased vision found in one eye in 14 patients (22%) and in both eyes in 3 (5%) was attributable to tumor.

Visual fields were normal in 76% of patients. An optic nerve-type defect was present in 16%, incomplete bitemporal hemianopia in 5%, and junctional scotoma in 3%. When papilledema occurred, it was found to be bilateral in 5% and unilateral in 3%. Unilateral optic atrophy was found in 11% of patients.

The initial ocular motility was normal in 38% of patients. The most common motility disturbance was isolated left sixth cranial nerve paresis, seen in 15 patients (24%). Next most common were bilateral sixth nerve paresis (10%), right sixth nerve paresis (5%), left third and sixth nerve pareses (5%), and unilateral third nerve paresis (5%). Two patients had total left ophthalmoplegia due to involvement of the third, fourth, and sixth nerves, and one patient had total left ophthalmoplegia secondary to orbital involvement by tumor. The remaining six patients had bilateral palsies with sixth nerve palsy on one side and either third nerve paresis or total ophthalmoplegia contralaterally. In all, 35 patients (56%) had sixth nerve paresis, 14 (22%) had third nerve paresis, and 5 (8%) had fourth nerve paresis, the fourth nerve paresis always in combination with third or sixth nerve paresis.

TABLE II: INITIAL OCULAR FINDINGS IN 63 PATIENTS WITH INTRACRANIAL CHORDOMA

Ocular finding	Number of patients		Percent	
Visual loss	17		27	
One eye		14		22
Both eyes		3		5
Visual field defect	15		24	
Optic nerve defect		9		14
Bitemporal hemianopia		3		5
Junctional scotoma		2		3
Unknown		1		2
Papilledema	5		8	
Both eyes		3		5
One eye		2		3
Unilateral optic atrophy	7		11	
Ocular motility disturbance	39		62	
Sixth nerve paresis		35		56
Third nerve paresis		14		22
Fourth nerve paresis		5		8
Lateral jerking nystagmus	6		10	
Sensory fifth nerve paresis	10		16	
Seventh nerve palsy	4		6	

Two patients had paresis of conjugate lateral gaze, presumably due to pontine compression by tumor. Six patients had lateral jerking nystagmus. Ten patients had involvement of one or more branches of the fifth cranial nerve, and four patients had seventh nerve involvement.

The site of origin of the tumors, as determined by radiographic means and surgical observations, was along the clivus in 58 patients (92%). In one patient the tumor appeared to arise within the sphenoid sinus, and in one patient, in the parasellar area. In three patients the site of origin could not be determined because of widespread tumor involvement.

Most of the patients were treated by surgery followed by radiation therapy or by surgery or radiation therapy alone. Usually, the ocular status was not immediately affected. By a small margin, more patients had an immediate benefit than had a loss of visual acuity, worsened strabismus, or loss of visual field.

DISCUSSION

The average age of 44 years of our patients is in general agreement with that noted in other series. Godtfredsen[2] noted that these tumors were most common in the age range of 25 to 45 years, and Allen and Kerr[3] had eight patients with an average age of 52. The male predominance found in our series has also been noted by other authors.

Early involvement of the sixth cranial nerve seems to be characteristic of chordoma.[1,2,4-6] The origin and growth pattern of this tumor are reflected in the frequency of the various ocular findings. The tumor arises from vestigial remnants of the notochord. The notochord is the axial supporting structure of the embryo, and it regresses as the bony skeleton develops; this leaves as normal remnants only the nuclei pulposi of the intervertebral spaces. Tissue remnants may be entrapped within bone in the dorsum sellae and along the clivus, where they occasionally undergo neoplastic transformation.

The most frequent site of extension of the tumors in our series was along the anterior clivus and over the petrous bone onto the floor of the middle fossa in the parasellar area. Anterior extension into the sella and ventral spread into the sphenoid sinus were almost as common. The palsies of the third, fourth, and sixth cranial nerves occurred predominantly in patients with tumor extension anteriorly. The sixth nerve is presumably vulnerable all along its course—through the subarachnoid space along the clivus, as it pierces the dura inferior to the petrosphenoidal ligament, as it passes over the petrous part of the temporal bone, and as it traverses the cavernous sinus.

Fewer patients had extension ventrally into the retropharyngeal space, posteriorly with brainstem compression, laterally into the cerebellopontine angle, and caudad toward the foramen magnum. In these patients, involvement of the third, fourth, and sixth cranial nerves was much less common.

There was a distinct tendency for left-sided cranial nerves to be involved. This tendency has been noted before,[7] but no explanation has been offered.

SUMMARY

Sixty-three patients with confirmed intracranial chordoma were studied retrospectively to determine the incidence of various presenting symptoms and signs. Most of the ocular signs were due to cranial nerve involvement. Sixth cranial nerve palsy occurred as the sole presenting sign in 29% of patients, whereas extraocular muscle palsies of various combinations were present in 62%. Visual field defects were demonstrated in 24% of patients, but only 19% had papilledema or optic atrophy. The chordomas arose from the clivus in 92% of patients, but different patterns of cranial nerve involvement occurred which correlated with the different sites of extension of the tumor.

REFERENCES

1. Heffelfinger MJ, Dahlin DC, MacCarty CS, et al: Chordomas and cartilaginous tumors at the skull base. *Cancer* 32:410, 1973.
2. Godtfredsen E: Eye and nerve symptoms in connection with cranial chordomas. *Acta Ophthalmol* 21:224, 1943.
3. Allen KL, Kerr WA: Chordomas of the clivus and the cervical spine. *S Afr Med J* 42:1165, 1968.
4. Miller SJH: Ocular signs of chordomas. *Proc R Soc Med* 65:522, 1972.
5. Falconer MA, Bailey IC, Duchen LW: Surgical treatment of chordoma and chondroma of the skull base. *J Neurosurg* 29:261, 1968.
6. Adenis JP, Robin A: Signes oculaires des chordomes spheno-occipitaux: a propos d'un cas. *Rev Otoneuroophtalmol* 47:129, 1975.
7. Walsh FB, Hoyt WF: *Clinical Neuro-ophthalmology*, ed 3, Baltimore, Williams & Wilkins Company, 1969.

DISCUSSION

Dr John Woodworth Henderson. The authors are to be complimented on a most thorough analysis of the ocular manifestations of chordoma.

It is this tumor which makes our early basic embryology study of the Amphioxus worthwhile, since it is embryonic rests of the primitive notochord which are thought to develop into chordomas.

These neoplasms are relatively rare. Givner in 1945 noted that less than 100 cases of spheno-occipital chordoma had been reported in the literature up to that time.

The Mayo Clinic series has been painstakingly accumulated over many years. A report in 1951 discussed only 15 spheno-occipital cases. By 1971 there were 55 cases, and the more recent total of 63 patients up to 1978 forms the basis of today's discussion. Therefore even in such an active referral center there was an accesion of only two cases per year from 1951 to 1971, and only eight more in the next seven years. Obviously one individual can rarely see more than a few, and accurate institutional records become of paramount importance.

Since few of us have the opportunity to evaluate the incidence of eye signs in chordomas, we should be truly grateful for the efforts of the authors.

Chordomas characteristically arise from remnants at the extreme ends of the notochord. The other main group not discussed in this paper is sacro-coccygeal and constitutes about two thirds of the total cases, with one third originating within the bone of the clivus. This ratio is true also in a series of 30 cases reviewed at the University of Michigan by Schneider, where 10 tumors were intracranial and 20 were spinal.

As the authors have pointed out, lesions arising from the clivus can produce multiple neurological complaints, but often present with diplopia (70%) and headache (57%). In the authors' series, 35 (or 56%) of the patients had sixth nerve involvement as part of their picture. Early involvement of one sixth

nerve (usually the left) was found in 29% and bilateral sixth nerve palsy in 10%. In addition, 5% showed a combination of left third and sixth nerve palsies, and unilateral oculomotor palsy occurred in another 5%.

As Givner noted in 1945: "unexplained paralysis of the lateral rectus muscle, more frequently the muscle on the left side, in a patient in his thirties with progression to chiasmic signs, headache preceding defects of the visual fields and no evidence of disorder of the pituitary should suggest chordoma."

When I first read this paper it immediately brought to mind a patient of over 30 years ago in which chordoma was high on our differential list. Since that time I have always considered chordoma of the clivus one of the few non-traumatic lesions which can produce bilateral sixth nerve palsy in the absence of increased intracranial pressure in its early stages.

This patient (slide), a 42-year-old woman, presented in 1948 with bilateral abducens palsies for which a cause could not be determined. Only after a year's interval did increasing headache and papilledema mandate further studies. Since the differential included basilar aneurysm, direct vertebral angiography was performed, and the patient expired a few hours later. At autopsy a tumor of the clivus was found, apparently arising from bone and extending from the pituitary nearly to the foramen magnum. However, the microscopic sections demonstrated a mucin-producing adenocarcinoma, similar to tissue obtained from a mastectomy several years before.

Since tumors of the clivus are difficult to identify in their early stages, I would like to ask the authors whether they have had any experience to indicate the value of the advanced forms of computerized scanning in these cases?

I would like to thank Doctor Bagan and Doctor Hollenhorst for a significant addition to our knowledge, and for their courtesy in sending the paper well in advance of the meeting. Further, I am indebted to them for a moment of nostalgia in harking back to the Amphioxus as my first introduction to the notochord in beginning embryology some 46 years ago.

Dr Thomas P. Kearns. I would like to congratulate Doctor Bagan on his fine presentation. I have two questions. First, the preponderance of left sided VI nerve involvement seems strange and I wonder if the laterality found by Doctors Bagan and Hollenhorst correlates with that noted by previous authors?

Secondly, it has been my experience that confronted by a patient with bilateral VI nerve involvement one should consider two likely possibilities. These are a malignancy of the paranasal sinuses or a clivus chordoma. The first may usually be excluded as it is a more acute condition and the patient often has pain, nose bleeds and diagnostic features. The clivus chordoma is more often asymptomatic. My question is, is there anything in your study to substantiate my feeling that the two most common causes of bilateral paralysis of the VI nerves are sinus malignancy and chordoma?

DR ROBERT W. HOLLENHORST. Thank you very much, Doctor Henderson and Doctor Kearns, for your discussions. The greatest advance in diagnosis of intracranial disease is the CT scan. It facilitates the identification of intracranial tumors, and chordoma is no exception. With respect to Doctor Kearns' question about the preponderance of left VI nerve palsies, many people have tried to solve that dilemma and nobody really has done so to date. Almost every series larger than about six cases has noted this interesting finding. If one were to ask what the two most common causes of bilateral VI nerve palsies are, I would come up with exactly the same answer as you have, that is, malignancy of the paranasal sinuses or chordoma; and the outstanding thing about the chordoma is that there is so little additional symptomatology accompanying it. One added comment concerns the so-called Heppelfinger tumor, formerly called chondrosarcoma. About six years ago it was discovered that this is really a chondroid chordoma rather than a chondrosarcoma and the prognosis is much better than for true chondrosarcomas, and even better than for ordinary chordomas. None of these are included in this paper but this is an interesting outgrowth of the interest at the Mayo Clinic in chordomas.